

CLAIMS

What is claimed is:

1. A Synthetic nuclease resistant antisense oligodeoxynucleotides having a nucleotide sequence selected from the group consisting of SEQ ID No:4 and SEQ ID No:6.

2. The synthetic nuclease resistant antisense oligodeoxynucleotides as set forth in claim 1 having phosphorothioate bonds linking between the four 3'-terminus nucleotide bases for providing nuclease resistance.

3. A pharmaceutical or medical composition comprising as active ingredient at least one synthetic nuclease resistant antisense oligodeoxynucleotide as set forth in claim 1 in a physiologically acceptable carrier or diluent.

4. The pharmaceutical composition as set forth in claim 1 comprising either SEQ ID No:4 or SEQ ID No:6 and at least one other non-control AS-ODN selected from Tables 1 and 2 wherein the percent inhibition is greater than 25%.

a Sub B1
5. A synthetic nuclease resistant antisense oligodeoxynucleotide ^{for} ~~capable of~~ selectively modulating human tumor necrosis factor alpha by targeting exon sequences flanking donor splice sites thereby regulating expression of TNF- α .

6. The synthetic nuclease resistant antisense oligodeoxynucleotides ~~having~~ a nucleotide sequence as set forth in claim 5 selected from the group consisting of SEQ ID No:4 and SEQ ID No:6.

Sub A3
7. A pharmaceutical composition for selectively modulating mammalian tumor necrosis factor alpha in a mammal in need of such treatment consisting of an effective amount of at least one active ingredient as set forth in claim 1 and a pharmaceutically physiologically acceptable carrier or diluent.

8. A pharmaceutical or medical composition comprising as active ingredient at least one synthetic nuclease resistant antisense oligodeoxynucleotides as set forth in claim 6 in a physiologically acceptable carrier or diluent.

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9. A pharmaceutical composition ^{which inhibits} ~~for modulating~~ human tumor necrosis factor alpha in a patient in need of such treatment consisting of

an effective amount of at least one active ingredient as set forth in claim 6 or a ribozyme comprising a sequence complementary to at least a portion of exon sequences flanking donor splice sites in TNF- α ; and

a pharmaceutically physiologically acceptable carrier or diluent.

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10. A method of ^{inhibiting} ~~modulating~~ expression of human tumor necrosis factor alpha in a mammal by administering a pharmaceutical composition as set forth in claim 5.

11. A DNA expression sequence comprising a transcriptional initiation region and a sequence encoding an oligonucleotide as set forth in claim 5.

12. A vector comprising a DNA sequence according to claim 11.

ADD A4

ADD B2